REMARKS

Claims 1-3 and 5-7 have been amended, and claims 4 and 8-16 have been cancelled without prejudice or disclaimer. Claims 1-3, 5-7, and 17-22 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 1, paragraph 3; page 4, paragraphs 2, 3, and 5; page 5, paragraph 1; and page 9, paragraph 2. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Election/Restriction

The Office Action states that the instant application contains two groups of inventions that are not so linked as to form a single general inventive concept under PCT Rule 13.1: (1) Group I, claims 1-7 and 17-22, which the Action states are drawn to reagents for detecting human papilloma virus DNA; and (2) Group II, claims 8-16, which the Action states are drawn to methods of detecting human papilloma virus DNA. The Action notes that in a telephone interview with Applicants' representative Huw Jones on April 5, 2002, the claims of Group I were provisionally elected with traverse. The Action states that Applicants are required, in accordance with 37 C.F.R. § 1.499, to affirm their provisional election in replying to this Action.

Pursuant to 37 C.F.R. § 1.499, Applicants elect to prosecute claims 1-7 and 17-22, which are designated as Group I, and which the Action states are drawn to reagents for detecting human papilloma virus DNA. Non-elected claims 8-16 have been cancelled without prejudice or disclaimer.

2. Objection to claim 4 under 37 C.F.R. § 1.75(c)

The Office Action contains an objection to claim 4 under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Action states that claim 4 does not further limit the products of claim 1 because it modifies only the intended use of the products of claim 1 but does not impose any further structural limitation on the claimed products.

Applicants have canceled claim 4 without prejudice or disclaimer, rendering this objection moot.

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3. Rejections of claims 1-7 and 17-22 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-7 and 17-22 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

The Action first asserts that claim 1 is indefinite for reciting the phrase "capable of specifically hybridizing," because it is not clear whether the claimed probes have the potential to specifically hybridize or do in fact hybridize to high-risk HPV DNA. The Examiner suggests that the amendment of claim 1 to read "which hybridize" would obviate this rejection.

Applicants, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention, have amended claim 1 to recite viral genomic DNA probes "that detectably hybridize." Applicants contend that amended claim 1 is not indefinite since it is clear that the recited viral genomic DNA probes hybridize to DNA from carcinogenic HPV types. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 1 is indefinite for reciting "high-risk HPV DNA" and "low-risk HPV DNA" because there is no art established standard for determining whether an HPV type is a high-risk type or a low-risk type, and because the claims do not set forth a standard by which to determine the relative risk level of a particular HPV DNA type. The Action notes, for example, that while the instant application describes HPV types 31, 33, and 51 as being high-risk types, these types are also known in the literature as medium-risk (*i.e.*, intermediate-risk) HPV types.

Applicants respectfully disagree with the Action's assertion that the instant application describes HPV types 31, 33, and 51 as being high-risk types. Applicants note that the instant application explicitly describes HPV types 31, 33, and 51 as being intermediate-risk types (page 1, paragraph 3). Moreover, Applicants contend that at the time U.S. Provisional Application No. 60/105,657 (the '657 application) was filed (*i.e.*, October 26, 1998; the instant application claims the benefit of priority of International Application No. PCT/US99/25109, which, in turn, claims the benefit of priority of U.S. Provisional Application No. 60/105,657), it was not uncommon for those of ordinary skill in the art to describe HPV types as being either high-risk or low-risk (essentially merging the intermediate-risk and high-risk groups), rather than as being high-risk, intermediate-risk, or low-risk (*see, e.g.*, Togawa *et al.*, 1995, *J. Med. Virol.* 45:435-38; Southern *et al.*, 1997, *Cancer Res.* 57:4210-13; Jacobs *et al.*, 1997, *J. Clin. Microbiol.* 35:791-95; and Gravitt *et al.*, 1998, *J. Clin.*

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Microbiol. 36:3020-27). In addition, Applicants note that at the time the '657 application was filed, it was not uncommon for those of ordinary skill in the art to describe the HPV types 31, 33, and 51 as high-risk types (*see, e.g.*, Southern *et al.*, 1997; Jacobs *et al.*, 1997; and Gravitt *et al.*, 1998). Applicants also note that at the time the '657 application was filed, the HPV types described in the instant application as being low-risk types (*i.e.*, 6, 11, 42, 43, and 44) were unequivocally understood by those of ordinary skill in the art to be low-risk types, and further, that types 40, 53, 54, and 57 were also understood by those of ordinary skill in the art to be low-risk types (*see, e.g.*, Southern *et al.*, 1997; Jacobs *et al.*, 1997; and Gravitt *et al.*, 1998).

Notwithstanding the fact that some skilled artisans employ an HPV classification scheme that separates HPV types into high-risk and low-risk categories, while other skilled artisans employ a classification scheme that separates HPV types into high-risk, intermediate-risk, and low-risk categories, Applicants contend that such classification schemes are merely shorthand ways of distinguishing HPV types which are known to be associated with malignancy (*i.e.*, carcinogenic HPV types) from HPV types which are known not to be associated with malignancy (*i.e.*, non-carcinogenic HPV types). Applicants contend that while those of ordinary skill in the art, depending on the particular classification scheme that they employ, might disagree as to whether a particular HPV type (*e.g.*, HPV types 31, 33, or 51) is high-risk or intermediate-risk, those of ordinary skill in the art would be able to recognize, or readily determine, whether a particular HPV type is carcinogenic or non-carcinogenic. Applicants, therefore, have amended claim 1 to recite "a plurality of viral genomic HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types but do not detectably hybridize to DNA from non-carcinogenic HPV types." Applicants contend that because amended claim 1 no longer recites the terms "high-risk HPV DNA" or "low-risk HPV DNA" and, more importantly, because one of ordinary skill in the art in view of the teachings in the instant specification and knowledge in the prior art would have been able to readily discern whether a particular HPV type is carcinogenic or non-carcinogenic, amended claim 1 is not indefinite. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 7 and 22 are indefinite because claim 7 recites a reagent in which "each DNA probe is present in the following amounts," but recites a series of percentages, and because the claim does not set forth of what (*e.g.*, hybridization mix, probe mix) the percentages are portions.

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Applicants have amended claim 7 to recite a reagent in which "the viral genomic DNA probes are present in the reagent in the following proportions." Applicants contend that because amended claim 7 no longer recites the term "amounts" in combination with a series of percentages, and recites that the percentages are portions of the reagent (or viral genomic DNA probe cocktail), amended claim 7 is not indefinite. Applicants, therefore, respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment, and request that the Examiner withdraw all rejections made on this basis.

4. Rejections of claims 1-7 and 17-22 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-7 and 17-22 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the claims do not set forth particular sequences for the probes of the claimed reagent and recite the probes only in terms of their function, the genus of reagents encompassed by the claims includes reagents comprising *any* probe that is specific to any HPV type that is known to cause cancer, and therefore, that the genus of reagents encompassed by the claims includes hundreds of thousands of possible reagents. Specifically, the Action states that the claims encompass reagents comprising any set of *oligonucleotide* probes that is specific to any HPV type that is known to cause cancer. The Action also states that because the specification defines "full length" as permitting some sequence variation and shortening of the probes in the claimed reagents, even claims that recite reagents comprising a set of full length probes encompass reagents comprising a set of *oligonucleotide* probes. The Action further states that because Applicants describe only a single reagent meeting the functional limitations of the claims, Applicants have express possession of only one species in a genus that comprises hundreds of millions of different possibilities.

As discussed in section 3 above, Applicants have amended claim 1 to recite "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types but do not detectably hybridize to DNA from non-carcinogenic HPV types" (*emphasis*

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added). Applicants also note that the instant specification describes the HPV probes of the invention as "*essentially full length genomic* HPV probes" having "*essentially* the same sequence as given in GenBank Accession Numbers: K02718 - type 16; X05015 - type 18; J04353 - type 31; M62877 - type 51; M12732 and A12360 - type 33; M74117 - type 35," and that "[w]hile some sequence variations and shortening of the probe length are permitted, *these are still considered full length and are not similar to oligonucleotide probes as used in the prior art*" (page 5, paragraph 1) (*emphasis added*). Applicants further note that the sequences described in GenBank Accession Nos. K02718, X05015, J04353, M62877, M12732, A12360, and M74117 range from 7808 to 7912 nucleotides in length, and that HPV-specific oligonucleotides described in the prior art usually range from 30 to 50 nucleotides in length (*see, e.g.*, International Publication No. WO 95/22626, discussed in section 5 below, which describes HPV-specific oligonucleotides of 23, 25, 28, and 30 nucleotides in length).

Applicants contend that because amended claim 1 recites a reagent comprising a plurality of viral *genomic* HPV DNA probes, the claimed reagent does not comprise *any* probe that is specific to any HPV type that is known to cause cancer. Applicants also contend that one of ordinary skill in the art, in view of the teachings of the instant application and knowledge in the prior art, would readily understand, for example, that an HPV 16-specific 28-mer oligonucleotide does *not* comprise an *essentially full length* genomic HPV probe having *essentially* the same sequence as that recited in GenBank Accession No. K02718. Applicants further contend that one of ordinary skill in the art would readily understand that a number of reagents comprising a plurality of viral genomic HPV DNA probes could be prepared using the teachings in the instant application and knowledge in the art at the time the instant application was filed.

In view of the teachings in the instant application, Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the claimed genus of reagents, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

5. Rejection of claims 1, 2, and 4-6 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1, 2, and 4-6 under 35 U.S.C. § 102(b), as

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being anticipated by International Publication No. WO 95/22626 (Meijer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose reagent s comprising smaller groupings of HPV probes. The Action further states that the probes disclosed by Meijer *et al.* are full length probes because Meijer *et al.* disclose the entire sequence of each probe and that the full length of the probe is to be used in preparing the reagent.

As discussed in section 4 above, the instant specification teaches that the HPV probes of the invention are "*essentially full length genomic* HPV probes" that "are *not* similar to oligonucleotide probes as used in the prior art" (page 5, paragraph 1) (*emphasis added*). As also described in section 4 above, Applicants have amended claim 1 to recite "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types but do not detectably hybridize to DNA from non-carcinogenic HPV types" (*emphasis added*). Applicants note that Meijer *et al.*, on the other hand, disclose *oligonucleotide* primers of only 23-28 nucleotides for amplifying HPV DNA present in a sample by polymerase chain reaction, and *oligonucleotide* probes of only 30 nucleotides for HPV genotyping of the amplification product. Applicants contend, therefore, that while the reagent of Meijer *et al.* comprises HPV-specific *oligonucleotide* probes, the reagent of amended claim 1 comprises viral *genomic* HPV DNA probes (*i.e.*, HPV-specific *polynucleotide* probes).

In addition, Applicants respectfully disagree with the Action's assertion that since Meijer *et al.* disclose the entire sequence of their probes and that the entire length of their probes are to be used, the probes disclosed by Meijer *et al.* are *full length* probes. Applicants contend that because Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides – or *only* about 0.38% of the HPV genome (*i.e.*, the HPV genome comprising nearly 8000 nucleotides) – Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, the genus of reagents defined by the pending claims does not encompass the oligonucleotide probe reagent disclosed by Meijer *et al.*, and therefore, Meijer *et al.* cannot anticipate claims 1, 2, and 4-6. Withdrawal of this rejection is therefore respectfully solicited.

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The Office Action also asserts a rejection of claims 1, 4, and 5 under 35 U.S.C. § 102(b), as being anticipated by Troncone *et al.*, 1992, *J. Clin. Pathol.* 45:308-313. The Action states that Troncone *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Troncone *et al.* disclose a reagent comprising full length genomic probes that are specific for HPV types 16, 18, and 33.

Applicants note that Troncone *et al.* disclose a non-isotopic *in situ* hybridization (NISH) study in which samples were first analyzed in *separate* hybridizations with "genomic HPV probes" corresponding to HPV types 6/11, 16, 18, and 33 (page 309), and then because no samples tested positive for HPV types 6 or 11 (page 312, Table 3), the samples were re-examined by hybridization with "[a] cocktail of HPV 16, 18, and 33 probes" (page 309). Applicants contend that because none of the samples analyzed by Troncone *et al.* tested positive for HPV types 6 or 11 (*i.e.*, non-carcinogenic types), it is not all at clear from the reference that the HPV 16/18/33 cocktail of Troncone *et al.* specifically hybridizes to *only* carcinogenic HPV types. Applicants contend, therefore, that because Troncone *et al.* does not teach a probe cocktail known to specifically hybridize to only carcinogenic HPV types, a probe cocktail that detectably hybridizes to DNA from a plurality of carcinogenic HPV types but does not detectably hybridize to DNA from non-carcinogenic HPV types does not "necessarily flow[] from the teachings of the applied prior art," as it is required to do to properly anticipate the pending claims. *Ex parte Levy*, 17 U.S.P.Q.2d (BNA) 1461, 1464 (B.P.A.I. 1990). Moreover, Applicants contend that while it is clear that Troncone *et al.*, in their initial analysis, used four genomic HPV probes (including a genomic probe that recognizes the non-carcinogenic HPV types 6/11), it is not at all clear that the probes in the HPV 16/18/33 cocktail were *genomic* probes, as opposed to *oligonucleotide* probes. Applicants contend that because Troncone *et al.* does not teach "a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types *but do not detectably hybridize to DNA from non-carcinogenic HPV types*" (*emphasis added*), Troncone *et al.* does not anticipate claims 1, 4, and 5. Withdrawal of this rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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6. Rejection of claims 3, 7, and 17-22 under 35 U.S.C. § 103

The Office Action asserts a rejection of claim 3 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,981,173 (Orth *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the probes taught by Orth *et al.* in the reagent taught by Meijer *et al.*

As discussed in section 5 above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. In addition, Orth *et al.* disclose oligonucleotide probes for the detection of HPV types 68 and 70, rather than essentially full length genomic probes. Applicants contend that because neither Meijer *et al.* nor Orth *et al.* disclose the use of essentially full length genomic probes, the genus of reagents defined by the pending claims does not encompass the oligonucleotide probe reagent disclosed by Meijer *et al.* in view of Orth *et al.*, and therefore, Meijer *et al.* in view of Orth *et al.* does not result in a *prima facie* case of obviousness with respect to claim 3. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claim 7 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,639,871 (Bauer *et al.*). The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that

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Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have experimented with different probe concentrations so as to arrive at an optimal concentration for the detection of HPV in a sample.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claim 7 does not encompass optimized hybridization assays that use the reagent disclosed by Meijer *et al.*, and therefore, Meijer *et al.* in view of Bauer *et al.* does not result in a *prima facie* case of obviousness with respect to claim 7. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 17, 18, 20, and 21 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of the 1988 Stratagene Catalog. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose reagent s comprising smaller groupings of HPV probes. The Action further states that the probes taught by Meijer *et al.* are full length probes because Meijer *et al.* disclose the entire sequence of each probe and that the full length of the probe is to be used in preparing the reagent. The Action also states that Meijer *et al.* do not disclose kits wherein the reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie*

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obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Meijer *et al.* into containers for distribution in a kit.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claims 17, 18, 20, and 21 do not encompass a kit containing the reagent disclosed by Meijer *et al.*, and therefore, Meijer *et al.* in view of the 1988 Stratagene Catalog does not result in a *prima facie* case of obviousness with respect to claims 17, 18, 20, and 21. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 17 and 20 under 35 U.S.C. § 103(a), as being unpatentable over Troncone *et al.*, 1992, *J. Clin. Pathol.* 45:308-313, in view of the 1988 Stratagene Catalog. The Action states that Troncone *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Troncone *et al.* disclose a reagent comprising full length genomic probes that are specific for HPV types 16, 18, and 33. The Action also states that Troncone *et al.* do not disclose kits wherein the reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Troncone *et al.* into containers for distribution in a kit.

As discussed in section 5 above, Troncone *et al.* disclose a non-isotopic *in situ* hybridization (NISH) study in which samples were first analyzed in *separate* hybridizations with "genomic HPV probes" corresponding to HPV types 6/11, 16, 18, and 33 (page 309), and then because no samples tested positive for HPV types 6 or 11 (page 312, Table 3), the samples were re-examined by hybridization with "[a] cocktail of HPV 16, 18, and 33 probes" (page 309). Applicants contend that because Troncone *et al.* does not teach a plurality of viral *genomic* HPV DNA probes that detectably hybridize to DNA from a plurality of carcinogenic HPV types *but do not detectably hybridize to DNA from non-carcinogenic HPV types*, claims 17 and 20 do not encompass a kit containing the reagent disclosed by Troncone *et al.*, and therefore, Troncone *et al.* in view of the 1988 Stratagene

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Catalog does not result in a *prima facie* case of obviousness with respect to claims 17 and 20. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claim 19 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,981,173 (Orth *et al.*), and further in view of the 1988 Stratagene Catalog. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent that hybridizes to HPV types 68 and 70, but that Orth *et al.* disclose the genomes of HPV types 68 and 70 and oligonucleotide probes for the detection of HPV types 68 and 70. The Action also states that Meijer *et al.* in view of Orth *et al.* does not disclose kits wherein the reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Meijer *et al.* in view of Orth *et al.* into containers for distribution in a kit.

As discussed above, neither Meijer *et al.* nor Orth *et al.* disclose the use of essentially full length genomic probes, and therefore, the combination does not result in a *prima facie* case of obvious. Applicants contend that because Meijer *et al.* in view of Orth *et al.* does not disclose the use of essentially full length genomic probes, claim 19 does not encompass a kit containing the reagent disclosed by Meijer *et al.* in view of Orth *et al.*, and therefore, Meijer *et al.* in view of Orth *et al.*, and further in view of the 1988 Stratagene Catalog, does not result in a *prima facie* case of obviousness with respect to claim 19. Withdrawal of this rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claim 22 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 95/22626 (Meijer *et al.*) in view of U.S. Patent No. 5,639,871 (Bauer *et al.*), and further in view of the 1988 Stratagene Catalog. The Action states that Meijer *et al.* disclose a reagent for detecting human papillomavirus DNA comprising a plurality of DNA probes capable of specifically hybridizing to high-risk HPV DNA but not low-risk HPV

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DNA. Specifically, the Action states that Meijer *et al.* disclose a reagent comprising probes specific for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 54, 56, and 58. The Action also states that Meijer *et al.* disclose that it is advisable to add a probe specific for HPV type 59 to the reagent, and that the reagent should be supplemented with additional probes as new high-risk HPV types are identified. The Action further states that Meijer *et al.* do not disclose a reagent comprising probes that are present in the proportions recited in claim 7, but that the optimization of hybridization assays by determining ideal probe concentrations was routine in the prior art at the time the invention was made (as exemplified by Bauer *et al.*). The Action also states that Meijer *et al.* in view of Bauer *et al.* does not disclose kits wherein the reagents are in containers, but that the 1988 Stratagene Catalog discloses the benefits to the practitioner of kits. The Action asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged the reagents taught by Meijer *et al.* in view of Bauer *et al.* into containers for distribution in a kit.

As discussed above, Meijer *et al.* disclose the use of HPV probes comprising only 30 nucleotides, or *only* about 0.38% of the HPV genome, and therefore, Meijer *et al.* does *not* disclose the use of essentially full length genomic probes. Applicants contend that because Meijer *et al.* does not disclose the use of essentially full length genomic probes, claim 22 does not encompass a kit containing the reagent disclosed by Meijer *et al.* for use in optimized hybridization assays, and therefore, Meijer *et al.* in view of Bauer *et al.*, and further in view of the 1988 Stratagene Catalog does not result in a *prima facie* case of obviousness with respect to claim 22. Withdrawal of this rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 103 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Switzer believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

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Respectfully submitted,

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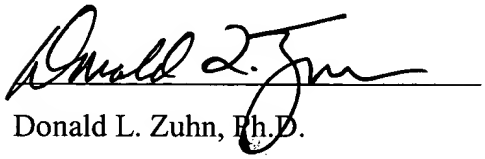
Dated: November 26, 2003

By: 

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